Evaluation of the efficacy of injectable platelet-rich fibrin in genitourinary syndrome of menopause

Pelin Oyardı[1], Ülkü Mete Ural[2]

[1]Department of Obstetrics and Gynecology, Baykan State Hospital, Siirt, Türkiye

[2]Department of Obstetrics and Gynecology, Bolu Abant İzzet Baysal University Faculty of Medicine, Bolu, Türkiye

Abstract

Objective: The aim of this study was to investigate the efficacy of injectable, platelet-rich fibrin (PRF) for the treatment of vaginal atrophy, also known as genitourinary syndrome of menopause (GSM), which may affect a third of a woman's lifespan.

Material and Methods: This study included postmenopausal patients who had symptoms of genitourinary syndrome, such as vaginal burning, dryness, itching, and sexual dysfunction. Injectable platelet-rich fibrin (i-PRF) was applied to three areas on the posterior vaginal wall twice, one month apart. The genitourinary symptoms of the patients were evaluated using the female sexual function index (FSFI) and sexual life quality questionnaire before and one and six months after the procedure.

Results: Thirty-five patients were recruited with a mean age of 54.1±5.5 years. The analysis of the desire, arousal, lubrication, orgasm, satisfaction, pain, and total scores of the pre-procedural and post-procedural FSFI and sexual life quality questionnaire scores revealed significant improvements ($p<0.001$).

Conclusion: i-PRF treatment provided advantages such as safe and easy application, autologous material nature, absence of procedure-related complications or side effects, short procedure time, absence of the need for hospitalization, low cost, and a non-hormonal nature. These results suggest that injectable, PRF may be a promising treatment option in patients with symptoms of GSM. However, larger randomized controlled studies are needed to confirm and validate our findings. (J Turk Ger Gynecol Assoc. 2025; 26: 15-9)

Keywords: Female sexual function, genitourinary syndrome, injectable platelet-rich fibrin, menopause, minimally invasive therapy

Received: 21 May, 2024 **Accepted:** 11 October, 2024 **Publication Date:** 12 March, 2025

Introduction

Changes in the vulva, vagina and urinary system due to a hypoestrogenic state resulting from the loss of ovarian function in the menopausal period are called vulvovaginal atrophy. However, it has been suggested that this term does not fully correspond to the symptoms. Therefore, the terminology was changed to genitourinary syndrome of menopause (GSM) at the annual meetings of the International Society for the Study of Women's Sexual Health and The North American Menopause Society (1,2).

Symptoms of GSM include dyspareunia, vaginal dryness, loss of lubrication, friable vaginal epithelium, vaginal bleeding and discharge, vestibular discomfort, vulvar burning and itching, urethral sensitivity, dysuria, urinary urgency, recurrent urinary tract infections, and sexual dysfunction of arousal and orgasm (3). These symptoms of GSM occur in more than 50% of postmenopausal women, having a negative impact on quality of life, social activity and sexual relationships (4). Various treatment modalities for GSM have been described (5-7). These include hormonal and non-hormonal methods, such as vaginal moisturisers, lubricants, and platelet concentrates.

Address for Correspondence: *Pelin Oyardı*
e-mail: *pelinoyard@gmail.com* ***ORCID:*** *orcid.org/0000-0001-6405-0259*

DOI: *10.4274/jtgga.galenos.2024.2024-5-6*

Cite this article as: *Oyardı P, Mete Ural Ü. Evaluation of the efficacy of injectable platelet-rich fibrin in genitourinary syndrome of menopause. J Turk Ger Gynecol Assoc. 2025; 26: 15-9*

Platelet rich plasma (PRP) is a first-generation platelet concentrate that appears like a weak fibrin mesh after the activation of centrifuged blood with thrombin and calcium (8). The additional use of anti-coagulants, which are found in PRP have been demonstrated to inhibit the wound healing process (9). Due to the disadvantages of PRP, platelet-rich fibrin (PRF) emerged as the second-generation equivalent blood product. Autologous 100% natural PRF is obtained by centrifuging blood without adding any anticoagulant (10,11). Compared to PRP, PRF releases a greater amount of growth factors which makes it perfect for stimulating tissue regeneration and growth (10). Injectable platelet-rich fibrin (i-PRF), the liquid preparation of PRF, has more platelets, white blood cells and a greater degree of cellular migration than PRF (12). However, it has been reported that there are side-effect and cost considerations when using PRF (13). In the present study, we aimed to investigate the efficacy of i-PRF in women with GSM (13). There have been studies examining the use of PRP in GSM (14,15). However, we were unable to find any publications investigating the efficacy of i-PRF for GSM.

Material and Methods

This study was carried out from May 2021 to July 2022 at a outpatient clinics of Obstetrics and Gynecology Department of a University Hospital. The study was approved by the Bolu Abant İzzet Baysal University Local Ethics Committee (approval number: 2021/103, date: 27/04/2021) and performed in accordance with the Helsinki Declaration. Postmenopausal women suffering from one or more GSM symptoms were included to the study. Prior to enrolment and treatment, all patients were informed of the study's purpose and methodology and provided written informed consent.

Asian patients who did not have any gynecological pathology, had started natural menopause at least three years prior to the study, and were sexually active heterosexuals were included in the study. Women with a diagnosis of metabolic and/or chronic inflammatory diseases, who had undergone gynecological abdominal or vaginal surgery, were using hormone replacement therapy, smokers, had an active vaginal infection, or had previously undergone vaginal treatment (such as with hyaluronic acid) for GSM were excluded from the study.

An 18 mL blood sample was withdrawn from each patient and put into two i-PRF tubes. The blood samples were then centrifuged at 700 rpm for 3 minutes (16). The upper layer of the tube was aseptically withdrawn into a syringe. The patients were positioned in the lithotomy posture and the i-PRF preparation was immediately injected at three different lateral points, side-by-side at 0.5-1 cm intervals into the posterior vaginal wall, 2-3 cm above the vaginal forchete. Approximately 1-2 cc i-PRF solution was injected at each point. The procedure was performed using 26 G 0.45 mm insulin syringes. The procedure was repeated twice with a 1-month interval.

The patients were interviewed face-to-face and evaluated using the Female Sexual Function Index (FSFI) and sexual life quality scale (SLQQ) questionnaires before the procedure and one month and six months after the i-PRF application.

The FSFI questionnaire consists of 19 close-ended questions related to sexual activity within the four weeks prior to the examination and includes six domains: sexual desire (questions number 1-2), sexual arousal (questions number 3-6), lubrication (questions number 7-10), orgasm (questions number 11-13), satisfaction (questions number 14-16) and pain (questions number 17-19). Points are assigned for each answer (1-5 and 0-5 for questions 1-2 and questions 3-19, respectively), the sum of the scores for the domain is multiplied by the domain factor, the six domain scores are added up, and the total score may vary from 2.0 to 36.0 points. The effect coefficients used for scoring the whole scale are 0.6 for sexual desire; 0.3 for sexual arousal and lubrication; and 0.4 for orgasm, satisfaction, and pain/discomfort. A score lower than 26.55 was interpreted as indicating a risk of sexual dysfunction (17).

In the present study, the satisfaction level of the participants was also evaluated using the SLQQ. This scale is scored using a six-point Likert type and consists of 18 items. Each item is expected to be answered considering sexual life in the last four weeks. The scale is evaluated by scoring each item with a score of 1-6 (1: I totally agree; 2: I largely agree; 3: I partly agree; 4: I partly disagree; 5: I largely disagree; 6: I totally disagree). The range of score of the scale is 18-108. In this scoring system, the total score obtained from the scale is converted to 100. It is reported that the formula (the raw score obtained from the scale-18, x100/90) must be used to convert the total scale score to 100. A high score indicates a good quality of sexual life (18).

Statistical analysis

The study data were analyzed using SPSS Statistics, version 26 (IBM Corp., Armonk, NY, USA). The descriptive statistics are presented as number of units (n), percentage (%), mean ± standard deviation mean (x ± SD), and/or median (M), minimum value and maximum value. Normality of scale score distribution was evaluated with skewness and kurtosis measures. For all difference scores, the kurtosis and skewness values were between -1.96 and 1.96, which proved that the data were normally distributed. The scale scores of all participants before the procedure and 1 month and 3 months after the procedure were analyzed using one-sided analysis of variance. The participants scale scores for body mass index (BMI), mode of delivery, and educational status before and 1 month and three months after the procedure were analyzed using two-sided analysis of variance for repeated measurements.

Bonferroni correction was used for all paired comparisons in analyses of variances in repeated measurements. A $p<0.05$ was considered statistically significant.

Results

A total of 35 postmenopausal women were included in this study, with the mean age of 54.15.5± years, ranging from 44-68 years and mean BMI was 29.68±6.79 kg/m^2, ranging 20.30-43.20. Thus less than a third (31.4%) exhibited normal weight while 37.2% were classified as obese. The duration of menopause was between 3 and 16 years, with a mean of 7.5±3.6 years. More than three-quarters (77.1%) had experienced at least one vaginal delivery. Demographic characteristics of the cohort are shown in Table 1.

There was an improvement in all parameters in the FSFI questionnaire after treatment (Table 2). Desire, arousal, lubrication, orgasm, satisfaction, pain, and total FSFI scores exhibited significant improvements. The scores of both the first and sixth months after the procedure were higher than the pre-procedure scores. However, there was no significant differences between the scores in the first and sixth months after the procedure.

Similarly, SLQQ questionnaire scores demonstrated significant improvement after i-PRF injection. Scores in the first and sixth months after the procedure were significantly higher than the pre-procedure scores. However, again there was no difference between the first and sixth months scores after the procedure (Table 3).

Table 1. Demographic data

Variables (n=35)	
Age (years)	54.1±5.5
BMI (kg/m^2)	29.68±6.79
Duration of menopause (years)	7.5±3.6
Number of children n (%)	
None	3 (8.6%)
One	2 (5.7%)
Two	18 (51.4%)
Three	7 (20.0%)
Four	5 (14.3%)
Mode of delivery n (%)	
None	3 (8.6%)
Normal	23 (65.7%)
Cesarean	5 (14.3%)
Normal + cesarean	4 (11.4%)
Educational status n (%)	
Illiterate	3 (8.6%)
Primary school	19 (54.3%)
High school	9 (25.7%)
University	4 (11.4%)
BMI: Body mass index	

Discussion

The diagnosis and treatment of the GSM are important for preventing progression and deterioration of the quality of life and sexual health. GSM affects from 40 to 54% of postmenopausal women (19). Alternative treatment methods, such as hyaluronic acid, laser and PRP are gaining popularity for the treatment of patients with GSM symptoms, such as breast and endometrial cancer, who cannot receive hormone therapy and who do not want to use hormone therapy (20). In the present study, vaginal i-PRF injection was found to be effective for improving symptoms of GSM.

PRP is a first-generation thrombocyte concentrate that is used as a regenerative agent. Compared to PRP, PRF has a higher wound healing enhancing effect because it releases a greater amount of growth factors. PRF stimulates tissue regeneration and growth by providing stable and constant release of the growth hormone and cytokines in the tissue. The advantage of PRF over PRP is that it is 100% natural and has no side effects because it is prepared without using anticoagulants or other biochemical additives.

PRF contains a larger number of white blood cells and thrombocytes, which are the key cells in wound healing, and a larger amount of fibrin. Thrombocytes provide regional activation of macrophages and neutrophils by releasing cytokines and growth factors (21). Leucocytes protect the wound against infections during wound healing and regulate the immune system by releasing cytokines, such as interleukin 1-beta (IL-1β), IL-6, IL-4, and tumor necrosis factor-alpha (22). Since PRF locks cytokines, glycolic chains, and structural glycoproteins in polymerized fibrin mesh, it affects the extracellular matrix, thereby promoting a reaction chain of endothelial cell migration, dislocation, and phenotype change, which ultimately results in new vessel formation (10).

i-PRF is the liquid form of PRF, and its three-dimensional fibrin content forms a system for regular release of growth factors. Due to this characteristic, i-PRF produces an excellent PRF thrombus substitute. Historically, the primary use of i-PRF was in oral maxillofacial surgery; however, its use has demonstrated significant success in both surgical and non-invasive esthetic procedures, leading to increased use in both esthetic and reconstructive medicine (23-25).

i-PRF has been used for skin rejuvenation, and the results indicated significant improvement due to its important regenerative functions, including stimulation of fibroblast proliferation through the mesenchymal stem cell pathway, enhanced anti-inflammatory effects, angiogenesis, and protein

Table 2. FSFI scores before treatment and 1, 6 months after treatment

FSFI	Pre-procedure	Post-procedure 1st month	Post-procedure 6th month	p
Desire	1.98 ± 0.9^{X}	2.97 ± 0.92^{Y}	2.71 ± 1.18^{Y}	**<0.001**
Arousal	1.56 ± 0.9^{X}	3.12 ± 1.20^{Y}	2.99 ± 1.30^{Y}	**<0.001**
Lubrication	1.26 ± 0.7^{X}	3.32 ± 1.34^{Y}	3.14 ± 1.45^{Y}	**<0.001**
Orgasm	1.35 ± 0.9^{X}	3.09 ± 1.31^{Y}	2.84 ± 1.27^{Y}	**<0.001**
Satisfaction	1.35 ± 0.8^{X}	3.06 ± 1.38^{Y}	2.99 ± 1.58^{Y}	**<0.001**
Pain	1.16 ± 0.7^{X}	3.45 ± 1.38^{Y}	3.21 ± 1.66^{Y}	**<0.001**
Total score	8.72 ± 4.5^{X}	19.04 ± 7.08^{Y}	17.88 ± 8.14^{Y}	**<0.001**

The data are summarized as mean ± SD. *One-sided analysis of variance in repeated measures. The upper case letters "X" and "Y" denote a significant difference between measurements. There is no statistical difference between the measurements denoted by the same letter. FSFI: Female sexual function index

Table 3. SLQQ scores before treatment and 1, 6 months after treatment

	Pre-procedure	Post-procedure 1st month	Post-procedure 6th month	p
SLQQ	35.15 ± 9.25^{X}	44.45 ± 11.3^{Y}	46.84 ± 13.7^{Y}	**<0.001**

The data are summarized as mean ± SD. *One-sided analysis of variance in repeated measures. The upper case letters "X" and "Y" denote a significant difference between measurements. There was no statistical difference between the measurements denoted by the same letter. SLQQ: Sexual life quality scale

accumulation for extracellular matrix remodeling through leukocytes (24). Furthermore, due to its ability to attract epithelial cells and facilitate microvascularization, PRF has the capacity to protect open wounds and expedite healing. Therefore, the application of PRF for periodontal diseases, particularly in dental root coverage, has become increasingly popular (25).

In a study conducted in 2024, the effects of i-PRF on stress urinary incontinence were investigated. Three consecutive i-PRF injections at one-month intervals into the mid-urethral location of the anterior vaginal wall was shown to effectively alleviate symptoms of stress urinary incontinence with high success rates, without any reported side effects (13).

Neto (26) recorded a decrease in the severity of dyspareunia and urinary incontinence after vaginal PRP injection. Runels et al. (14) performed a similar study with a single application and found a decrease in the rate of sexual dysfunction. Sukgen et al. (15), in a study involving 52 patients analyzed the effects of PRP injection to the anterior vaginal wall on genital perception in women with impaired orgasm and sexual dysfunction. These authors found an increase in the FSFI score and a high satisfaction level (15). Aguilar et al. (27) assessed the quality of sexual life after injecting hyaluronic acid and PRP to the posterior vaginal wall and reported a positive impact of the treatment in these patients. It was shown that symptoms of GSM significantly improved following hyaluronic acid and PRP injection in a study including 236 women (19). Similarly, a study found that PRP treatment could be used not only for the treatment of urinary incontinence, but also to treat the symptoms of vaginal fistula and the genitourinary syndrome (28). Numerous studies have shown that PRP (14,15,27) are effective in treating GSM. However, we were unable to find any published study of the efficacy of locally administered i-PRF for GSM. In the present study, i-PRF was injected twice at one-month intervals to the posterior vaginal wall at three separate but close sites. We did not detect any adverse conditions such as bleeding, pain, or allergic reactions at the injection site after the procedure. Significant improvements were detected in scores reported by both the FSFI and SLQQ, although the total scores for FSFI indicated all women still maintained a risk of sexual dysfunction, based on previously reported cut-offs.

Study Limitations

The limitations of our study include the lack of a standardized application procedure for the dose, application frequency, injection site, and number of injections of i-PRF. In addition, the number of cases was low, and there was no control group. Finally, the follow-up period was relatively short at six months and one of the questionnaires used had indicated a continued improvement at six months, although not significantly better than at three months follow-up. The fact that more than 77% of the patients included in the study had a vaginal birth and the average BMI of the patients was 29 are the factors that may affect the interpretation of the study results.

Conclusion

This study demonstrated that i-PRF application provided a significant improvement in sexual quality of life among women

with GSM symptoms measured by two validated questionnaires. i-PRF, which promotes angiogenesis, tissue regeneration, and wound healing, may have a role in the treatment of GSM. However, there is a need for longer term, larger prospective studies. These should also investigate the effects after more and/or larger doses of i-PRF, potentially monitoring the changes in the vaginal wall with biopsy, and using different indices, such as the vaginal health index.

Ethics

Ethics Committee Approval: *The study was approved by the Bolu Abant İzzet Baysal University Local Ethics Committee (approval number: 2021/103, date: 27/04/2021).*

Informed Consent: *All patients were written informed consent.*

Footnotes

Author Contributions: *Surgical and Medical Practices: P.O., Ü.M.U., Concept: P.O., Ü.M.U., Design: P.O., Ü.M.U., Data Collection or Processing: P.O., Ü.M.U., Analysis or Interpretation: P.O., Ü.M.U., Literature Search: P.O., Ü.M.U., Writing: P.O., Ü.M.U.*

Conflict of Interest: *No conflict of interest is declared by the authors.*

Financial Disclosure: *The authors declared that this study received no financial support.*

References

1. Portman DJ, Gass ML; Vulvovaginal Atrophy Terminology Consensus Conference Panel. Genitourinary syndrome of menopause: new terminology for vulvovaginal atrophy from the International Society for the Study of Women's Sexual Health and the North American Menopause Society. Menopause. 2014; 21: 1063-8.
2. Angelou K, Grigoriadis T, Diakosavvas M, Zacharakis D, Athanasiou S. The genitourinary syndrome of menopause: an overview of the recent data. Cureus. 2020; 12: e7586.
3. Sarmento ACA, Costa APF, Vieira-Baptista P, Giraldo PC, Eleutério J Jr, Gonçalves AK. Genitourinary syndrome of menopause: epidemiology, physiopathology, clinical manifestation and diagnostic. Front Reprod Health. 2021; 3: 779398.
4. Farrell Am E. Genitourinary syndrome of menopause. Aust Fam Physician. 2017; 46: 481-4.
5. Kagan R, Kellogg-Spadt S, Parish SJ. Practical treatment considerations in the management of genitourinary syndrome of menopause. Drugs Aging. 2019; 36: 897-908.
6. Palacios S, Mejía A, Neyro JL. Treatment of the genitourinary syndrome of menopause. Climacteric. 2015; 18(Suppl1): 23-9.
7. Cox S, Nasseri R, Rubin RS, Santiago-Lastra Y. Genitourinary syndrome of menopause. Med Clin North Am. 2023; 107: 357-69.
8. Mohan SP, Jaishangar N, Devy S, Narayanan A, Cherian D, Madhavan SS. Platelet-rich plasma and platelet-rich fibrin in periodontal regeneration: a review. J Pharm Bioallied Sci. 2019; 11: S126-30.
9. Zhang W, Guo Y, Kuss M, Shi W, Aldrich AL, Untrauer J, et al. Platelet-rich plasma for the treatment of tissue infection: preparation and clinical evaluation. Tissue Eng Part B Rev. 2019; 25: 225-36.
10. Kobayashi E, Flückiger L, Fujioka-Kobayashi M, Sawada K, Sculean A, Schaller B, et al. Comparative release of growth factors from PRP, PRF, and advanced-PRF. Clin Oral Investig. 2016; 20: 2353-60.
11. Dohan DM, Choukroun J, Diss A, Dohan SL, Dohan AJ, Mouhyi J, et al. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part II: platelet-related biologic features. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006; 101: e45-50.
12. Karde PA, Sethi KS, Mahale SA, Khedkar SU, Patil AG, Joshi CP. Comparative evaluation of platelet count and antimicrobial efficacy of injectable platelet-rich fibrin with other platelet concentrates: an in vitrostudy. J Indian Soc Periodontol. 2017; 21: 97-101.
13. Ural ÜM. The effect of injectable platelet rich fibrin as a nonsurgical treatment of the female stress urinary incontinence. Arch Gynecol Obstet. 2024; 309: 2229-36.
14. Runels C, Melnick H, Debourbon E, Roy L. A Pilot study of the effect of localized injections of autologous platelet rich plasma (PRP) for the treatment of female sexual dysfunction. J Women's Health Care. 2014; 3: 169.
15. Sukgen G, Ellibeş Kaya A, Karagün E, Çalışkan E. Platelet-rich plasma administration to the lower anterior vaginal wall to improve female sexuality satisfaction. Turk J Obstet Gynecol. 2019; 16: 228-34.
16. Wend S, Kubesch A, Orlowska A, Al-Maawi S, Zender N, Dias A, et al. Reduction of the relative centrifugal force influences cell number and growth factor release within injectable PRF-based matrices. J Mater Sci Mater Med. 2017; 28: 188.
17. Rosen R, Brown C, Heiman J, Leiblum S, Meston C, Shabsigh R, et al. The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. J Sex Marital Ther. 2000; 26: 191-208.
18. Symonds T, Boolell M, Quirk F. Development of a questionnaire on sexual quality of life in women. J Sex Marital Ther. 2005; 31: 385-97.
19. Moccia F, Pentangelo P, Ceccaroni A, Raffone A, Losco L, Alfano C. Injection treatments for vulvovaginal atrophy of menopause: a systematic review. Aesthetic Plast Surg. 2023; 47: 2788-99.
20. Lubián López DM. Management of genitourinary syndrome of menopause in breast cancer survivors: an update. World J Clin Oncol. 2022; 13: 71-100.
21. Tonnesen MG, Feng X, Clark RA. Angiogenesis in wound healing. J Investig Dermatol Symp Proc. 2000; 5: 40-6.
22. Eming SA, Brachvogel B, Odorisio T, Koch M. Regulation of angiogenesis: wound healing as a model. Prog Histochem Cytochem. 2007; 42: 115-70.
23. Karimi K, Rockwell H. The benefits of platelet-rich fibrin. Facial Plast Surg Clin North Am. 2019; 27: 331-40.
24. Hassan H, Quinlan DJ, Ghanem A. Injectable platelet-rich fibrin for facial rejuvenation: a prospective, single-center study. J Cosmet Dermatol. 2020; 19: 3213-21.
25. Eren G, Atilla G. Platelet-rich fibrin in the treatment of localized gingival recessions: a split-mouth randomized clinical trial. Clin Oral Investig. 2014; 18: 1941-8.
26. Neto JB. O-shot: platelets rich plasma in intimate female treatment. J Women's Health Care. 2017; 6: 395.
27. Aguilar P, Hersant B, SidAhmed-Mezi M, Bosc R, Vidal L, Meningaud JP. Novel technique of vulvo-vaginal rejuvenation by lipofilling and injection of combined platelet-rich-plasma and hyaluronic acid: a case-report. Springerplus. 2016; 5: 1184.
28. Prodromidou A, Grigoriadis T, Athanasiou S. Platelet rich plasma for the management of urogynecological disorders: the current evidence. Curr Opin Obstet Gynecol. 2022; 34: 396-401.